REMARKS

The application has been amended. In particular, claims 1-6, 32-34, 44-47, and 51-53 have been canceled, and claims 57-64 have been added to more clearly define the present invention. The new claims include subject matter from Groups I and II, which Applicants are requesting be considered together. For example, Claim 57 includes subject matter from claims 2, 4, 5, 32 and 44, now canceled. Claim 58, 59 and 60 include subject matter from canceled claims 45, 46 and 6, respectively. Claim 61 incorporates subject matter from claims 4 and 33, now canceled. Claim 62 includes subject matter from canceled claims 4 and 34. Claims 63 and 64 have been added in response to a suggestion made by the Examiner in the final Office Action mailed October 15, 2004.

It is noted that although claim 33 was withdrawn by the Examiner, Applicants believe this is a mistake, since claim 33, now canceled, was among the claims grouped in the present restriction requirement.

RESPONSE TO RESTRICTION REQUIREMENT

The Examiner has withdrawn the restriction requirement as set forth in the Office Action mailed February 5, 204. In the final Office Action mailed October 15, 2004, the Examiner has required election of one of groups I-XII, which are alleged as being distinct inventions. In particular, in the interest of advancing prosecution, the Examiner has attempted to group the claims according to drug type, and the action of the drug.

In response, Applicants respectfully request that the subject matter of Groups I and II be considered together for reasons that will now be described. In particular, both anisomycin and sparsomycin are drugs considered to be of the same class of antibiotics. In particular, based on their structures, both drugs are considered in the art to belong to the class of aminoacylated nucleoside antibiotics. Also, the present inventors have found that both anisomycin and

sparsomycin modulate the efficiency of programmed -1 ribosomal frameshifting, thereby suppressing viral propagation. Whereas sparsomycin increases the efficiency of programmed -1 ribosomal frameshifting, and anisomycin decreases it, the final result of these drugs is the same. For purposes of the present invention, the important point is that the efficiency of programmed -1 ribosomal frameshifting is changed, resulting in a suppression of the propagation of viruses that use this frameshift mechanism.

For similar reasons, applicants believe that the subject matter of claim 32 (now canceled), which is incorporated into new claim 57, should be entitled to examination in the instant application.

The new claims include subject matter from Groups I and II, which Applicants are requesting be considered together. In the event that the Examiner does not agree to consider both Groups I and II, Applicants elect to pursue the subject matter of Group II.

Objections to the Specification

The application has been amended to update the status of the prior nonprovisional patent application as abandoned. Moreover, Figs. 1A and 1B have been amended. Therefore, the objections to the specification have been addressed by the amendments presented herewith.

Claim Rejections-35 U.S.C. §112, Second Paragraph

The Examiner has maintained his rejections of claims 1-4 and claims 32, 34, 44-47, 51 and 53 under 35 U.S.C. §112, second paragraph. These rejections have been addressed in the language of new claims 57-64.

Claim Rejections-35 U.S.C. §112, First Paragraph

Written Description Rejection

The Examiner has maintained the written description rejection of claim(s) 1-3, 5, 32, 34, 44-46, 51 and 53 under 35 U.S.C.§112, first paragraph for reasons of record stated in the Office Action mailed May 14, 2004, and in the final Office Action mailed October 15, 2004.

In the Office Action mailed May 14, 2004, the Examiner alleged that the specification was limited to anisomycin and sparsomycin as examples of drugs, and that it failed to provide any additional representative species of the recited genus of drugs. In response, Applicants argued that the disclosure is not limited to anisomycin and sparsomycin as the specification teaches several examples of other compounds which are encompassed by the claims. However, in the final Office Action, the Examiner is of the opinion that even in view the additional representative examples, these representative examples fail to represent the entire genus of drugs encompassed by the claims.

These rejections will be addressed with respect to the new claims, which include subject matter from the rejected claims.

In order to advance prosecution of the present application, new claim 57 recites "exposing eukaryotic cells to a compound selected from the group consisting of anisomycin and sparsomycin." In view of the language that has been adopted for claim 57, Applicants respectfully request withdrawal of the written description rejections.

Enablement Rejection

The Examiner has maintained the scope of enablement rejection of claims 1-6, 32, 34, 44-47, 51 and 53 under 35 U.S.C. §112, first paragraph for reasons of record stated in the Office Action mailed May 14, 2004, and in the final Office Action mailed October 15, 2004.

The Examiner alleges that the specification fails to enable the full scope of the claims, and that the claims are so broad as to encompass *in vivo* methods of treating a vast number of diseases using any drug that modulates programmed ribosomal frameshifting, for example. Also, he alleges that the specification does not enable a skilled artisan to practice the full scope of the claimed methods *in vivo*.

These rejections will be addressed with respect to the new claims, which include subject matter from the rejected claims.

New claim 57 recites a method for treating infections caused by viruses using programmed -1 ribosomal frameshifting. Support for this language can be found, for example, at page 35, lines 7-32, page 59, lines 13-33 to page 60, lines 1-9 and page 64, lines 7-13 of the application. Moreover, claim 57 recites the use of a compound selected from anisomycin or sparsomycin, wherein the compound modulates the efficiency of programmed -1 ribosomal frameshifting, thereby suppressing viral propagation. As mentioned above, this modulation includes increases, as well as decreases in the efficiency of programmed -1 ribosomal frameshifting. Either way, the final result of these drugs is the same. For purposes of the present invention, the important point is that the efficiency of programmed -1 ribosomal frameshifting is changed, resulting in a suppression of the propagation of viruses using this frameshift mechanism.

Applicants submit that the specification enables a skilled artisan to practice the full scope of the method of new claim 57 *in vivo*.

For example, Applicants have provided at least three working examples which show that anisomycin and sparsomycin alter the efficiency of programmed -1 ribosomal frameshifting *in vivo* in viruses which utilize programmed -1 ribosomal frameshifting. The *in vivo* assays show

anisomycin and sparsomycin operating in a cellular environment reflective of the milieu where such compounds would be required to operate.

Also, Applicants have provided suitable concentration ranges at page 16, lines 26-30 of the specification. As evidenced from the figures (see, for example Figure 8), these concentrations effectively modulated programmed -1 ribosomal frameshifting in eukaryotic cells harboring viruses using programmed -1 ribosomal frameshifting.

Applicants disclosure also provides data demonstrating that anisomycin and sparsomycin cause meaningful deductions in HIV titers. For example, Figure 15A shows that anisomycin/sparsomycin concentrations of 1 ng/ml reduce HIV titers in human cells by about 70-80%.

Moreover, from the standpoint of a skilled clinician, the antibiotic compositions are known, and suitable modes of antibiotic administration would be readily determined by the skilled clinician, depending on the site of the viral infection, and the known structure of the antibiotic. For example, well known modes for antibiotic administration include oral, intravenous, intramuscular, and topical administrations.

Also, a skilled clinician is well aware that the use of antibiotic therapy as a therapeutic is reasonably predictable, and antibiotic therapy is a mature science. As the Examiner has acknowledged, actual success in treating humans or animals is not required for patentablity.

In view of the adopted language in the new claims, and the arguments presented herewith, Applicants respectfully request withdrawal of the enablement rejections.

Claim Rejections Under 35 U.S.C. §102 and 35 U.S.C. §102/103

The Examiner has maintained the rejection of claims 1-5, 32, 34, 44-46, 51 and 53 under 35 U.S.C. §102 (b), as allegedly being anticipated by Japanese Patent JP 63146818A, as evidenced by Dinman, et al. The Examiner has also maintained the rejection of claims 6 and 47 under 35 U.S.C. §102 (b), as allegedly anticipated by or, in the alternative, under 35 U.S.C. §103 (a) as obvious over JP 63146818A, as evidenced by Dinman, et al.

These rejections will be addressed together with respect to the new claims.

New claim 57 recites the following: "treating eukaryotic infections caused by viruses using programmed -1 ribosomal frameshifting by exposing eukaryotic cells to a compound selected from the group consisting of anisomycin and sparsomycin, wherein the compound modulates the efficiency of programmed -1 ribosomal frameshifting, thereby suppressing viral propagation in the cells."

In contrast to the present invention, the JP patent does not teach, disclose or suggest the use of anisomycin or any other compound to treat viral infections caused by viruses using programmed -1 ribosomal frameshifting. The JP patent, at best, provides a general teaching to use anisomycin to treat infections resulting from a laundry list of viruses, including both RNA and DNA viruses, many of which do not use programmed -1 ribosomal frameshifting.

A general teaching to use anisomycin to treat any virus as provided by the JP Patent actually teaches away from the present invention. For example, the present inventors have found that anisomycin or sparsomycin cannot be used to treat just any virus. In particular, the present inventors have found that anisomycin and sparsomycin, while being useful for treating viral infections caused by viruses using the -1 ribosomal frameshifting, are not effective for treating viral infections caused by viruses using +1 ribosomal frameshifting (e.g., see page 59, lines 13-18 of the application). The present inventors have shown that neither of these drugs alters the

efficiency of +1 ribosomal frameshifting in eukaryotic cells harboring Ty1, which is the yeast equivalent of a retrovirus which uses a ribosomal frameshift in the +1 direction for the production of its Gag and Gag-Pol proteins. Therefore, contrary to the express teachings of the JP Patent, Applicants have found that anisomycin is not effective against just any virus, and that it will not work on some of the viruses included in the families listed in the JP Patent.

Moreover, contrary to assertions made by the Examiner in the final Office Action, the JP Patent does not in any way enable a method for *in vivo* treatment of HIV infection using anisomycin. As shown in Exhibit A, there are many families of DNA viruses and RNA viruses of differing structure. However, many of these families do not use programmed -1 ribosomal frameshifting. Even certain viruses within Retroviridae do not use -1 ribosomal frameshifting. A review of the English portions of the JP Patent indicates that they provide only two working examples (see page 143). These examples are directed to treatment of infections from coxsackie virus and herpes simplex virus (HSV), neither of which use programmed -1 ribosomal frameshifting. In particular, coxsackie virus is a member of the Picornaviridae family of RNA viruses, and herpes simplex virus belongs to the Herpesviridae family of DNA viruses. Neither of these families use programmed -1 ribosomal frameshifting. Also, a laundry list disclosure of practically every RNA and DNA virus would not reasonably lead those skilled in the art to viruses using programmed -1 ribosomal frameshifting. Therefore, the JP Patent is not an enabling reference for use against the invention as presently claimed. Furthermore, that which might be enabled in the JP Patent (treatment of coxsackie and herpes simplex infections) directs you in a direction which is not claimed, since the coxsackie virus and the herpes simplex virus don't use programmed -1 ribosomal frameshifting.

Furthermore, that which is inherent in the prior art, if not known at the time of the invention, cannot form a proper basis for rejecting the claimed invention. Before Applicants discovered the effect of anisomycin and sparsomycin on viruses using programmed -1 ribosomal

frameshifting, nothing in the art suggested employing these compounds against viruses using this frameshift mechanism.

Finally, in moving from the prior art to the claimed invention, one cannot base a determination of patentability on what the skilled person might try or find obvious to try. Rather, the proper test requires determining what the prior art would have led the skilled person to do. "Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *Id.* at 473, 5 U.S.P.Q.2d at 1531. Applicants submit that the JP Patent, at best, would lead the skilled person to use anisomycin as a general anti-viral agent, or as an agent effective against coxsackie virus and herpes simplex virus. It would not have led the skilled artisan to use anisomycin or any other compound as an agent to treat viruses using programmed -1 ribosomal frameshifting given the lack of enablement. In fact, that which may be enabled in the JP Patent (treatment of coxsackie and herpes simplex infections) would lead the skilled artisan in a direction which is not claimed, since these viruses do not use programmed -1 ribosomal frameshifting.

As mentioned above, the present inventors have found that anisomycin and sparsomycin are particularly effective at treating infections caused by viruses using -1 ribosomal frameshifting over those caused by viruses that don't employ this mechanism. Further in this regard, Applicants note that Figure 15A of the present application shows that anisomycin/sparsomycin concentrations of only 1 ng/ml are effective to reduce HIV titers in human cells by about 70-80%, whilst the tables in the JP Patent appear to show that at least 0.125 μg/ml (i.e., 100x more) anisomycin is required to have a similar effect on herpes or coxsackie virus levels.

The Examiner has relied upon the Dinman, et al. reference for evidence showing that anisomycin is a peptidyl transferase inhibitor. The Dinman, et al. reference was published more than 1 ½ years after Applicants' earliest priority date and is based, in part, on the present invention. It is noted that before Applicants' invention, the public was not in possession of the

method recited in new claim 57. Therefore, no further discussion is believed necessary with regard to the Dinman, et al. reference.

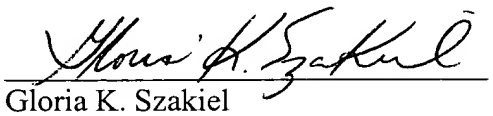
In view of the language of the new claims, and the arguments presented herewith, Applicants respectfully request withdrawal of these rejections.

Summary

Applicants submit that the claims, as presently recited, are patentably distinct over the art and allowable in form. An allowance of the claims is respectfully requested. Should the Examiner have any questions concerning this response, he is encouraged to contact the undersigned agent.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461.

Respectfully submitted,



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Amendments to the Drawings:

The attached two sheets of drawings include changes to Figs. 1A and 1B. These sheets replace the original sheets including Figs. 1A and 1B. In particular, applicants have amended Fig. 1A and Fig. 1B to include references to sequence identifier Nos. 6 and 15, respectively. Applicants have also amended Figs. 1A and 1B to remove references to EF-1, EF-2 and peptidyl transferase, which are well known proteins involved in the steps of protein synthesis.